

2. Claims 51-55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent 5,122,464.

While not agreeing with this rejection, Applicants respectfully submit that a terminal disclaimer may be provided upon indication that the pending claims are allowable.

3. Claims 56-58 stand rejected under 35 USC § 112, second paragraph, as being indefinite in the recitation of "reduced". The Examiner asserts that the term "reduced" is subjective and could include a cell which produces 99.99% of normal GS activity.

Applicants respectfully traverse this rejection and submit that the definition of "reduced" is clear to anyone reading the specification because this term has a well recognized definition. For instance, Webster's New World Dictionary (3rd College Edition) defines "reduced" as "to lessen in any way, as in size, weight, amount, value, price, etc.; diminish" (a copy of this page is attached as exhibit A).

The Examiner states that this term could encompass cells which produce 99.99% of normal GS activity to cells producing 0.001% of normal GS activity. Applicants respectfully agree with the Examiner that the term "reduced" encompasses the stated levels of GS activity. Applicants respectfully direct the Examiner to the preamble of claim 56 which recites: "A method of endowing a cell line with the ability to survive in a medium

(08/302,241)

lacking glutamine...". According to this limitation of claim 56, it is the vector which endows the cell line with the ability to survive in glutamine-free medium. Therefore, the endogenous levels of glutamine are not an issue.

Applicants respectfully submit that the level of endogenous GS activity is not a limiting factor in the claimed method as vector encoded GS is a dominant selectable marker wherein cells expressing endogenous levels of GS can be selected against by the use of GS inhibitors such as Msx (see page 9, first paragraph of the specification). Applicants have shown that selection for gene amplification using Msx leads almost exclusively to the isolation of clones in which the vector-derived GS gene has been amplified over the endogenous gene (see page 9, second paragraph of the specification).

Applicants respectfully submit that the test for indefiniteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. Miles Laboratories, Inc. v. Shandon Inc., 27 USPQ2d 1123, 1126, 997 F.2d 870 (Fed. Cir. 1993). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112, second paragraph demands no more. Id. Given this test for indefiniteness and the fact that GS is a dominant selectable marker, the recitation of "reduced" levels of GS in the claimed method of endowing a cell line with the ability to survive without glutamine cannot be held to be

(08/302,241)

indefinite. Accordingly, Applicants respectfully request withdrawal of the above identified rejection.

CONCLUSIONS

In view of the above discussion and Amendments, Applicants respectfully submit that the application is considered to be in condition for allowance. The Examiner is invited to call the undersigned attorney if any minor matter remains.

Respectfully submitted,



John W. Schneller
(Registration No. 26,031)
SPENCER & FRANK
1100 New York Avenue, N.W.
Suite 300E
Washington, D.C. 20036
Telephone: (202) 414-4000
Telefacsimile: (202) 414-4040

JWS:MST:dvb

(08/302,241)

Exhibit A

THIRD COLLEGE EDITION

Webster's New World Dictionary

OF AMERICAN ENGLISH

VICTORIA NEUFELDT

Editor in Chief

DAVID B. GURALNIK

Editor in Chief Emeritus



Webster's New World
Cleveland & New York

reducer / reeky

1126

reducere, to lead back < *re-*, back + *ducere*, to lead: see **DUCT** 1 a) to lessen in any way, as in size, weight, amount, value, price, etc.; diminish b) to put into a simpler or more concentrated form 2 to bring into a certain order; systematize 3 to break up into constituent elements by analysis 4 a) to put into a different form (to reduce a talk to writing) b) to change to a different physical form, as by melting, crushing, grinding, etc. 5 to lower, as in rank or position; demote; downgrade 6 a) to bring to order, attention, obedience, etc., as by persuasion or force b) to subdue or conquer (a city or fort) by siege or attack 7 a) to bring into difficult or wretched circumstances (a people reduced to poverty) b) to compel by need to do something (reduced to stealing) 8 a) to weaken in bodily strength; make thin (reduced to skin and bones) b) to thin (paint, lacquer, etc.), as with turpentine 9 *Arith.* to change in denomination or form without changing in value (to reduce fractions to their lowest terms) 10 *Chem.* a) to decrease the positive valence of (an element or ion) b) to increase the number of electrons of (an atom, element, or ion) c) to remove the oxygen from; deoxidize d) to combine with hydrogen e) to bring into the metallic state by removing nonmetallic elements 11 *Phonet.* to articulate (a vowel) in a central position, giving it a neutral quality, as in an unstressed syllable 12 *Photog.* to weaken or lower the density of (a negative or print) by removing metallic silver 13 *Surgery* to restore (a broken bone, displaced organ, etc.) to normal position or condition —*vi.* 1 to become reduced 2 to lose weight, as by dieting —**SYN.** DECREASE —**reduc'ible** *adj.* —**reduc'ibly** *adv.*

re-duc'er (-ər) *n.* 1 a person or thing that reduces 2 *Mech.* a fitting for connecting two pipes of different size 3 *Photog.* a solution that dissolves silver, used to decrease the density of a negative or positive image

reducing agent any substance that reduces another substance, or brings about reduction, and is itself oxidized in the process

reducing glass a biconcave lens used for reducing the visual size of something viewed through it

reduc-tase (ri duk'tās', -tāz') *n.* [REDUCT(ION) + -ASE] any of a class of enzymes that catalyze biochemical reductions

reduc-tio ad ab-sur-dum (ri duk'tē ō' ad ab sur'dam, -shē ō') [L. reduction to absurdity] *Logic* the proof of a proposition by showing its opposite to be an obvious falsity or self-contradiction, or the disproof of a proposition by showing its consequences to be impossible or absurd

reduc-tion (ri duk'shan) *n.* [LME *reduc-tion* < MFr *reduc-tion* < L *reduc-tio* < *reduc-tus*, pp. of *reducere*] 1 a reducing or being reduced 2 anything made or brought about by reducing, as a smaller copy, lowered price, etc. 3 the amount by which anything is reduced —**reduc'tional** *adj.*

reduction division MEIOSIS (sense 1)

reduc-tion-ism (-iz-əm) *n.* any method or theory of reducing data, processes, or statements to seeming equivalents that are less complex or developed: usually a disparaging term —**reduc'tion-ist** *n.*, *adj.* —**reduc-tion-is'tic** *adj.*

reduc-tive (ri duk'tiv) *adj.* [ML *reduc-tivus*] 1 of or characterized by reduction or reductionism 2 reducing or tending to reduce —**reduc'tively** *adv.*

reduc-tor (-tər) *n.* *Chem.* any apparatus for carrying out the reduction of metallic ions in solution for purposes of analysis; specif., a long tube filled with granular zinc for reducing a ferric solution to its ferrous salt

re-dun-dan'cy (ri dūn'dan sē) *n.*, *pl.* -cies [L *redundantia*] 1 the state or quality of being redundant; superfluity 2 a redundant quantity; overabundance 3 the use of redundant words 4 the part of a redundant statement that is superfluous 5 [Brit., etc. (exc. Cdn.)] discharge from a job or employment because of not being needed; dismissal Also **re-dun'dance**

re-dun-dant (-dant) *adj.* [L *redundans*, prp. of *redundare*: see REDOUND] 1 more than enough; overabundant; excess; superfluous 2 using more words than are needed; wordy 3 unnecessary to the meaning: said of words and affixes 4 [Brit., etc. (exc. Cdn.)] laid off from work as no longer needed; discharged; dismissed —**SYN.** WORDY —**re-dun'dantly** *adv.*

re-du-pli-cate (ri dū'plā kāt', -dyōō'; for *adj.* & *n.*, usually, -kit) *vt.* -cat'ed, -cat'ing [L *reduplicatus*, pp. of *reduplicare*: see RE- & DUPLICATE] 1 to redouble, double, or repeat 2 a) to double (a root syllable or other element) so as to form an inflected or derived form of a word (as *tom-tom*), sometimes with certain changes, as of the vowel (as in *chitchat*) b) to form (words) by such doubling —*vi.* to be or become reduplicated —*adj.* 1 reduplicated; doubled 2 VALUATE (sense 2a) —*n.* something reduplicated

re-du-pli-ca-tion (ri dū'plā kā'shan, -dyōō-) *n.* [LL *reduplicatio*] 1 a reduplicating or being reduplicated 2 something produced by reduplicating, as a word containing a reduplicated element 3 the element added in a reduplicated word form —**re-du'pli-ca'tive** *adj.*

re-du-vi'd (ri dū'vē id, -dyōō') *n.* [ModL *Reduviidae* < L *reduvia*, hangnail, remnant < OL *reduvia* < **reducere*, to strip away < *red-*, RE- + *ducere* < IE base **deu-*, to put on] ASSASSIN BUG

re-dux (rē'duks') *adj.* [L < *reducere*: see REDUCE] that has been brought back, revived, restored, etc.

red-ware (rēd'wer') *n.* [RED + *ware*, seaweed < ME *war* < OE < IE **woiso-*, twig, wand, rod < base **wei-*, to twist, bend > WIRE] any of several large, brown, leathery, edible kelps (genus *Laminaria*)

red water TEXAS FEVER

red wine any wine made from dark, purplish grapes when the grape

skins are left with the juice after pressing to allow the absorption of reddish coloring agents during fermentation

red-wing (-wīn') *n.* 1 a small European thrush (*Turdus iliacus*) with an orange-red patch on the underside of the wings 2 RED-WINGED BLACKBIRD

red-winged blackbird a North American blackbird (*Agelaius phoeniceus*) with a bright-red patch on each wing near the shoulder in the male Also **redwing blackbird**

red-wood (-wood') *n.* 1 a giant evergreen (*Sequoia sempervirens*) of the baldcypress family, having fire-resistant bark, enduring, wood, and needlelike leaves: found in coastal regions of California and S Oregon 2 BIG TREE 3 any of a number of trees with reddish wood or yielding a red dye 4 the wood of any of these trees

Redwood City city in W Calif., on San Francisco Bay: suburb of San Francisco: pop. 55,000

Redwood National Park national park in NW Calif., containing groves of redwood trees: 170 sq. mi. (440 sq. km)

red worm BLOODWORM

re-echo or **re-echo** (rē ek'ō) *vt.*, *vi.* -ech'loed, -ech'loing to echo back or again; resound —*n.*, *pl.* -ech'loes the echo of an echo Also **re-echo**

rechy (rē'chē) *adj.* **rechy'er**, **rechy'est** [LME *rechy* < ME *rechy* < var. of *rek*, REEK] [Now Chiefly Dial.] smoky, dirty, foul, or razed

reed (rēd) *n.* [ME *rede* < OE *hreed*, akin to OHG *hriot* < IE base

**kreut-*, to shake, tremble] 1 a) any of various tall, slender grasses (esp. genus *Phragmites*), with plumelike inflorescences, growing in wet or marshy land b) the stem of any of these grasses c) such plants or stems collectively, specif. as material for thatching, basketwork, etc. 2 a rustic musical instrument made from a hollow stem or stalk and played by blowing through it 3 an ancient Hebrew unit of linear measure equal to 6 cubits: Ezek. 47:3 4 a device on a loom, by means of which threads are drawn between the separated threads of the warp 5 [Old Poet.] an arrow 6 *Archit.* a small, rounded molding: reading 7 *Music* a) a thin strip of wood, flexible substance, as cane, placed against the opening of the mouthpiece of certain wind instruments, as the clarinet, so as to leave a narrow opening: when vibrated by the breath, it produces a musical tone b) an instrument with a reed or reeds c) in some organs, et sim. device that vibrates in a current of air —*vt.* to thatch or decorate with reeds

Reed (rēd) 1 John 1887-1920; U.S. journalist & radical 2 Walter 1851-1902; U.S. army surgeon & bacteriologist

reed-bird (-būrd') *n.* *dialect name* for BOBOLINK

reed-buck (-būk') *n.*, *pl.* -buck' or -buck's [transl. of Du *riedbok*, any of a genus (*Redunca*) of small African antelopes with spread hooves and, in the males, backward-sloping, ringed horns turned inward and forward near the tips]

reed-ing (-in) *n.* 1 a small, rounded, decorative molding 2 a set of such moldings, as on a column 3 knurling along the edge of a

reed instrument any instrument whose sound is produced by vibrating reed or reeds, including, specif., the oboe, clarinet, saxophone, English horn, and bassoon

reed mace Brit. name for CATTAIL

reed organ an organ with a set of free metal reeds instead of pipes to produce the tones: cf. REED PIPE

reed pipe an organ pipe in which the tone is produced by a current of air striking a vibrating reed in an opening in the pipe: cf. FLUTE

reed stop 1 a set of reed pipes (in an organ) operated by one knob

re-edu'cate or **re-edu'cate** (rē ej'ə kāt') *vt.* -cat'ed, -cat'ing to educate again or anew, esp. so as to rehabilitate or adapt to new situations —**re-edu'ca'tion** or **re-ed'u'ca'tion** *n.* —**re-ed'u'ca'tive** *adj.*

reedly (rēd'ē) *adj.* **reed'ly'er**, **reed'ly'est** 1 full of reeds 2 made of reeds or reeds 3 like a reed; slender, fragile, etc. 4 sounding like a reed; thin: piping —**reed'ly** *adv.* —**reed'ly-ness** *n.*

reef (rēf) *n.* [prob. via Du or MLow *rif* < ON, lit., RIB] 1 a ridge of rock, coral, or sand lying at or near the surface of the water 2 *Mining* a bed or vein of ore; lode —**SYN.** SHOAL

reef (rēf) *n.* [ME *rif* < ON *rif* < IE **reip-*, a strip or cord] 1 to tear, cut > RIVE: orig. used of cords for reefing] 2 a part of a sail which can be folded or rolled up and made fast to reduce the area exposed to the wind, as during a storm —*vt.* to reduce the size of (a sail) by taking in part of it 2 to lower (a mast) or reduce the projection of (a bowsprit)

reefer (rē'fər) *n.* 1 a person who reefs 2 a short, thick, double-breasted coat in the style of a seaman's jacket 3 [from the appearance of a reef (of a sail)] [Slang] a marijuana cigarette [altered contr. of REFRIGERATOR] [Slang] a refrigerator truck, ship, etc.

reef knot a square knot used for reefing sails

reek (rēk) *n.* [ME < OE *rec*, akin to ON *reykr*, Ger *rauch*, < IE **reug-*, cloud, smoke] 1 vapor; fume 2 a strong, unpleasant stench 3 [Scot. or North Eng.] smoke —*vi.* [ME *reken* < OE

can.] 1 to give off steam or smoke 2 to have a strong, unpleasant smell 3 to be permeated with anything very unpleasant expose to the action of smoke or fumes 2 to emit or exude (fumes, etc.) —**reek'ly** *adj.*

OBOE REED (SIDE VIEW)

OBOE REED (TOP VIEW)

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS

CLARINET MOUTHPIECE WITH REED (SIDE VIEW)

REEDS